REMARKS

Claims 1-33 have been cancelled and new claims 34-74 have been added to more distinctly claim that which Applicants regard as their invention. These new claims are supported by the specification and therefore are not new matter.

Claims 1-5, and 19-26 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to an animal model for a human pathogen, particularly a non-chimpanzee animal model or a primate animal model. As a human being is not a chimpanzee, the claims encompass human beings which are non-statutory subject matter. See MPEP 2105. Inclusion of the term "non-human" would be remedial.

Claims 1-5 and 7-9 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to an animal model for a human pathogen, particularly a non-chimpanzee animal model. Simian immunodeficiency virus (SIV) is closely related evolutionarily to HIV-2 and more distantly related to HIV-1. SIV infection of macaques is used as a model system for HIV-1 infection of humans. For a discussion, see Lewis et al. (1995). Lewis et al. state on p. 146, paragraph 2, that "[p]athologic findings in infected macaques...share many similarities with those seen in HIV-1 infected humans." SIV-infected macaques are a product of nature and are therefore non-statutory subject matter. Thus, the claims read on non-statutory subject matter.

Claims 1-5 and 7-9 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to an animal model for a human pathogen, particularly a non-chimpanzee animal model.

Feline immunodeficiency virus (FIV) is a natural pathogen in cats. FIV infection of cats is used as a model system for HIV-1 infection of humans. For a discussion see Lewis et al. (1995). Lewis et al. state on p. 145, paragraph 4, that "FIV infection of cats is an attractive lentivirus model" and "[t]here are several similarities between FIV in cats and HIV-1 in humans." FIV-infected cats are a product of nature and are therefore non-statutory subject matter. Thus, the claims read on non-statutory subject matter.

Claims 6, 18, and 30 are rejected under 35. U.S.C.101 because the claimed invention is directed to non-statutory subject matter. Claim 6 is directed to products or processes developed or derived from the animal model. Claim 18 is similarly drawn to "products or processes." Claim 30 is directed to a "product or procedure." The statute allows for obtaining a patent for either a product or a process. Multiple distinct classes of statutory subject matter cannot be claimed in a single claim. Products are processes are separate classes of inventions and therefore are properly the subject matter of separate claims.

Claims 31-33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 31-33 are directed to "cells, tissues or organs" derived from the claimed animal models. The statute allows for obtaining a patent for a composition of matter in the singular form. Multiple distinct compositions of matter cannot be claimed in a single claim. Cells, tissues, and organs are distinct, each form the other, and therefore are properly the subject matter of separate claims. Furthermore, as the claimed animals read on a product of nature for the reasons discussed above, the claimed cells, tissues, and organs also read on a product of nature, which is non-statutory subject matter.

The claims do not require that the cells, tissues, or organs comprise a non-native pathogen.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *Tupaia belangeri* infected with HIV or HBV, does not reasonably provide enablement for any animal model of any species for any and all human pathogens. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to an animal model for a human pathogen.

The specification fails to provide an enabling disclosure for any animal model for any human pathogen. The claims encompass any animal species as a model for any human pathogen. However, the specification only discloses *Tupaia belangeri* as an animal model for HBV and HIV infections. No guidance is offered with regard to how one skilled in the art would develop other animal models for human pathogens. No other human pathogens were examined for their capacity to infect any animal species. No other animal species were examined for their susceptibility to any human pathogen. There are numerous human pathogens including bacterial, viral, protozoan, and parasitic pathogens. There are half a million animal species including insects, worms, mammals, amphibians, reptiles, fish, birds, spiders, marsupials, etc. No guidance is offered with regard to the numerous parameters that must be examined to determine if one or more of the half million species of animals is susceptible to infection by a single human pathogen. Furthermore, genetic modification may be used to render an animal susceptible to infection by a human pathogen. The claims encompass genetically modified animals, but the

specification does not disclose any genetic modifications that could be made to render a given animal susceptible to infection by a given human pathogen. The instant specification only deals with two viral pathogens and their infectivity in a single species of animal. Animal models of human infectious disease are notoriously unpredictable as evidenced by the numerous attempts to product or identify a suitable animal model for HIV infection (see Lewis et al., 1995). Lewis et al. (1995) discuss the many problems that exist with regard to the disease characteristics displayed by the best animal models for HIV infection. None of the animal models exhibit the ideal characteristics as outlined in Box 1, page 144. Thus, despite an enormous amount of data on the HIV virus and its role in causing AIDS and despite intense effects to generate an adequate animal model, significant deficiencies remain.

Given the lack of specific guidance in the specification with regard to generating or identifying animal models for human pathogens, the limited working examples disclosed, and the unpredictability in the art for developing animal models of human infectious diseases, one skilled in the art would have been required to engage in undue experimentation to produce the claimed animal models and to use the animal models in the claimed methods.

Claims 1-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the full scope of the claimed invention.

The claims are directed to an animal model for a human pathogen. Claim 6 is directed to products or processes developed or derived from the animal model.

Claim 18 is directed to a therapeutic or disease-preventive drug or product or diagnostic products or processes developed or derived from the animal model. Claims 27-29 are directed to a method for developing or screening therapeutic, preventive, or diagnostic products and procedures using the animal model. Claim 30 is directed to a therapeutic, preventive or diagnostic product or procedure obtained by an undisclosed method that uses the claimed animal model. Claims 31-33 are directed to cells, tissues or organs derived from the animal models.

The claims encompass any animal species as a model for any human pathogen. However, the specification only discloses two animal model systems. Tupaia belangeri were shown to be susceptible to infection by HBV and HIV-1. No other human pathogens were examined for their capacity to infect any animal species. No other animal species were examined for their susceptibility to any human pathogen. There are numerous human pathogens including bacterial, viral, protozoan, and parasitic pathogens. There are half a million animal species including insects, worms, mammals, amphibians, reptiles, fish, birds, spiders, marsupials, etc. Furthermore, genetic modification may be used to render an animal susceptible to infection by a human pathogen. The claims encompass genetically modified animals, but the specification does not disclose any genetic modifications that could be made to render an animal susceptible to infection by a human pathogen. The instant specification only deals with two viral pathogens and their infectivity in a single species of animal. Thus, the specification does not disclose a representative number of model systems that include a representative number of animal species in combination with a representative number of human pathogens. In analyzing whether a written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In this case, only two animal models are

disclosed. Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. In this case, no other relevant identifying characteristics have been disclosed. The specification does not teach a generally applicable methodology than can be used to identify animal species that can be productively infected with a given human pathogen. This limited information regarding the claimed embodiments is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of the full scope of animal models at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

With regard to the claimed products, processes, therapeutic products, diagnostic products, disease-preventive drug, method for developing or screening, cells, tissues, and organs, no written description is provided. The specification does not disclose any product or process developed or derived from any animal model as claimed. Even as relates to the disclosed Tupaia animal models, no products, drugs, or screening methods are disclosed as such. The absence of any written description of products, processes, drugs, and screening methods does not satisfy the written description requirements for the claimed genus. Some description of cells, tissues, and organs for the Tupaia models is disclosed with the analysis of the infection of the animal. However, this is not sufficient to constitute written description for cells, tissues, and organs for all animal models of human pathogens. Since there is not sufficient written description for the animal models, for the reasons discussed above, there likewise is not sufficient written description for their cells, tissues, and organs for the same reasons. The limited information regarding the claimed cells, tissues, and organs is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of

the full scope of cells, tissues, and organs at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

Rejections under the 35 U.S.C. § 112, Second Paragraph

Claims 1-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5, 7-17, and 19-26 are indefinite in their recitation of "secondary disease manifestation" because the specification does not define a "secondary disease manifestation". The specification states on page 2, lines 6-7 that "secondary manifestations can include inflammation, fibrosis, induced auto-immunity, apoptosis and cancer." These are non-limiting examples of potential secondary manifestations, but do not serve to define what a secondary manifestation actually is. The specification also refers to "primary and secondary disease manifestations" (p.7, lines 18-19), but does not distinguish one from the other. One skilled in the art would not know what constitutes a secondary disease manifestation. Thus, the metes and bounds of the claims are not clearly set forth.

Claims 1-5, 7-17, and 19-26 are indefinite because it is unclear if the claimed animal is actually infected with a human pathogen. For example, in Claim 10 it is unclear if the lower primate is actually infected with a human retrovirus. Animal models of human infectious disease often are not infected with a human pathogen, but rather are infected with a related pathogen for which the animal

species is a natural host. For example, primates infected with SIV are often used as a model system for HIV infection.

Claim 2 is indefinite in its recitation of "is capable of responding to therapeutic or preventive measures in said animal model to said secondary disease manifestation" because it is unclear how "to said secondary disease manifestation" makes sense in this context. Is it the secondary disease manifestation that is treated or is the animal a model of the secondary disease manifestation?

Claims 3-5, 17, and 26 are indefinite because it is unclear how the recited intended use is further limiting. Intended use is not treated as a claim limitation unless it results in a further structural limitation. The metes and bounds of the claim are not clearly set forth.

Claim 8 is indefinite in its recitation of "comprises" because it is unclear how a viral pathogen can "comprise" e.g. HIV. Use of the term "comprises" implies that the pathogen can be made up of more than one part. However, a pathogen is a single, distinct entity that cannot be subdivided into parts. A "pathogen" refers to a whole pathogen and therefore cannot "comprise" HIV plus something else. Substitution of "is" for "comprises" is recommended. Furthermore, the claim is indefinite in its recitation of "combination of any of the foregoing" because a viral pathogen cannot be a combination of distinct viral pathogens.

Claim 9 is indefinite in its recitation of the phrase "wherein said non-viral pathogen comprises a bacterium." First, as discussed in the preceding paragraph, "comprises" cannot be used in its context because a bacterium is a non-viral pathogen and therefore cannot be only a part of a pathogen as implied by the use

of the term "comprises". Second, it is unclear if the claim is intended to be limited to bacterium because the wording of claim 7 allows for the pathogen to be viral or non-viral, and the further claim limitation in claim 9 only limits the non-viral pathogen but does not actually require that the pathogen be limited to said non-viral pathogen. The claim language is confusing because it still allows for the pathogen to be viral.

Claims 11, 12, 20 and 21 are indefinite in their recitation of "comprises" for the reasons discussed above. Furthermore, Claim 12 is indefinite in its recitation of "a combination of any of the foregoing" because HIV or HTLV cannot be a combination.

Claims 13 and 22 are indefinite in their recitation of "comprising Tupaia" because an animal cannot comprise anything more than one animal. Use of the phrase "wherein the lower primate belongs to the genus Tupaia" is recommended.

Claims 17 and 26 are indefinite in their recitation of "direct and indirect disease manifestation" because the specification does not define a direct or indirect disease manifestation, nor does it distinguish one from the other. The metes and bounds of the claims are not clearly set forth.

Claim 18 is indefinite because it is unclear whether the drug or product or diagnostic product or process is aimed at treating or diagnosing the infection of the animal model.

Claims 27-29 are indefinite because there are no method steps.

Rejections Under 35 U.S.C. § 102

The following art rejections relate to embodiments encompassed by the claims but not actually contemplated in the instant specification. Thus, while numerous animal models for a human pathogen exist in the prior art, the scope of enablement indicated on page 4 of this action relates only to the scope for which the instant specification is enabling and does not address enabled embodiments known in the prior art, as the prior art embodiments were not contemplated by Applicants.

Claims 1-5, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Barnett et al. (1994).

The claims are directed to an animal model for a human pathogen, particularly a non-chimpanzee animal model.

Barnett et al. (1994) disclose that baboons infected with HIV-2 exhibit an AIDS-like condition. Six baboons were intravenously inoculated with HIV-2. All seroconverted within 6 weeks after inoculation and five animals became persistently infected. Four developed lymphadenophathy, and three showed $CD4^{+}$T cell loss.

Thus, the claimed invention is disclosed in the prior art.

Claims 1-5, 7, 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Yan et al. (1996).

The claims are directed to an animal model for a human pathogen, particularly a non-chimpanzee animal model.

Yan et al. (1996) disclose that Tupaia belangeri can be experimentally infected with human hepatitis B virus (HBV). Infection can be prevented by immunization with hepatic B vaccine.

Thus, the claimed invention is disclosed in the prior art.

Claims 1-5, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Walter et al. (1996).

The claims are directed to an animal model for a human pathogen, particularly a non-chimpanzee animal model.

Walter et al. (1996) disclose that Tupaia belangeri are susceptible to infection with HBV.

Thus, the claimed invention is disclosed in the prior art.

Claims 1-5, 7, and 8 are rejected under 35 U.S.C. 102 (b) as being anticipated by Agy et al. (1992).

The claims are directed to an animal model for a human pathogen, particularly a non-chimpanzee animal model.

Agy et al. (1992) demonstrated that pig-tailed macaques are susceptible to infection with HIV-1.

Thus, the claimed invention is disclosed in the prior art.

Claims 1-5, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Mosier et al. (1991).

The claims are directed to an animal model for a human pathogen, particularly a non-chimpanzee animal model.

Mosier et al. (1991) demonstrated that the hu-PBL-SCID mouse is susceptible to infection with HIV-1.

Thus, the claimed invention is disclosed in the prior art.

Claims 1-5, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Namikawa et al. (1988).

The claims are directed to an animal model for a human pathogen, particularly a non-chimpanzee animal model.

Namikawa et al. (1988) disclose that the SCID-hu mouse is susceptible to infection with HIV-1.

Thus, the claimed invention is disclosed in the prior art.

Claim 9 is rejected under 35 U.S.C.102 (b) as being anticipated by Kuby (1991).

The claim is directed to an animal model for a human pathogen, wherein said pathogen is viral or non-viral, and wherein said non-viral pathogen comprises bacterium.

Kuby discloses on page 496 that SCID mice can be infected with Borrelia burgdorferi, the causative agent of Lyme disease, and once infected, SCID mice develop the disease.

Thus, the claimed invention is disclosed in the prior art.

Applicants respectfully traverse all of the Examiner's rejections. Applicants believe that the changes in the language of the claims should place them in condition for allowance. They have made it clear that although they are using an animal model as a host, they are using the human pathogen (and not a non-human pathogen surrogate) as the infectious agent.

Applicants have further limited the nature of the animal model to a lower primate. They have referred to the animal models in the specification using various terms such as "lower primate and primate excluding the order anthropoidea" (pgs. 1, 17), "primitive primate" (pg. 3),"lower primate" (pgs. 4, 7, 20), "a primate excluding any members of the Anthropoidea" (pg. 4), "such primate not including or excluding any members of the primate order Anthropoidea" (pg. 7), "a primate that is not a member of the suborder anthropoidea" (pg. 8), "a primate not belonging to the suborder Anthropoidea" (pg. 10), and "primate model not belonging to the suborder Anthropoidea" (pg. 20).

Primates are divided up into the suborders Anthropoidea and Prosimii; these are alternatively known as higher primates and lower primates respectively. As such, any member of the order "primate" that is not a member of the suborder Anthropoidea can collectively be referred to either as a lower primate or member of the suborder Prosimii. Applicants have chosen to use the positive term "lower primate" in the revised set of claims rather than the rather unwieldy term "primate not belonging to the suborder anthropidea".

With regard to the recitation of "secondary disease manifestations" the specification offers guidance to its meaning that is more complete than the two particular quotations offered by the Examiner. Specifically, page 2, lines 2-7 of the

specification state: "There may also be secondary manifestations of the infection that are not directly related to the propagative processes of the pathogens themselves. For instance, a cytopathic virus can kill cells directly, but a non-cytopathic virus can indirectly kill cells by inducing a host immune response that is responsible for death of the infected cell. Other secondary manifestations can include inflammation, fibrosis, induced auto-immunity, apoptosis, and cancer." Additionally, page 2, lines 26-28 of the specification state: "Although disease may be caused by replication of a pathogen, there may be other indirect or secondary manifestations that can be host specific."

It is clear from these passages in the specification that secondary manifestations are disease symptoms other than those directly caused by replication of the pathogen itself. Page 6, lines 17 and 18 of the specification state: "First, the models are capable of exhibiting analogous secondary disease manifestations." This serves as an indication that the particular secondary disease manifestations in the animal model are similar to those seen in a human after infection.

Although the original claims involved prevention and/or treatment, we have limited the present set of claims to treatment only.

The Examiner had also objected to claims 6, 18 and 30 since they involved products and processes together. We have eliminated these claims.

The Examiner had previously objected to claims 31-33 with reference to a recitation of "cells, tissues or organs". A dependent claim has been submitted where "cells, tissues or organs" are infected. This particular claim is directed

towards the concept that in addition to *in vivo* testing with an animal, various subcomponents that make up an animal may be suitable for testing *in vitro*.

The Examiner has previously objected to claims that were characterized as "any animal model of any species for any and all human pathogens". The present set of claims includes Claim 1 which is limited to lower primates as the animal model, and HCV and human retroviruses as the human pathogens. The present set also includes Claim 17 which is limited to lower primates as the animal model. Claim 17 also has the limitation that the therapy is directed towards "secondary disease manifestations". Accordingly, this claim is only operative in terms of human viral pathogens that exhibit secondary disease manifestations.

The Examiner states that certain claims are indefinite because they incorporate the word "comprises". The Manual of Patent Examining Procedure, section 2111.03 defines the transitional term "comprising" as "synonymous with 'including, containing, or characterized by', ...[as] inclusive or open-ended and does not exclude additional, unrecited elements or method steps". Furthermore, "'[c]omprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim." As such, Applicants use the word comprises as a transitional term to include additional entities, elements, or steps, and not to subdivide into parts.

Favorable reconsideration of this application as amended is respectfully requested. No fee or fee(s) are believed to be due in connection with this Amendment. In the event that any other fee or fees are due, however, in connection with the filing of this Amendment, authorization is

further given to charge the amount of any such fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that she be contacted at the number provided below.

Respectfully submitted,

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